

20/501838

24348-501NATL.ST25
SEQUENCE LISTING

<110> Ben-Sasson, Shmuel A.
Cohen, Einat

<120> Amino Acid Sequences Capable of Facilitating Penetration Across a
Biological Barrier

<130> 24348-501 NATL

<140> US 10/501,838

<141> 2003-02-07

<150> PCT/IB03/00968

<151> 2003-02-07

<150> US 60/355,396

<151> 2002-02-07

<160> 72

<170> PatentIn version 3.2

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<213> Haemophilus influenzae

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<213> Pasteurella multocida

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Leu Val Gln Gln Leu Ala
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Ser Ala Arg Leu Val Gln Gln Leu Ala Gly Gly Gly Lys Gly Gly Lys
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Asn Xaa

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Xaa Xaa Xaa Xaa Xaa Xaa Xaa
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Xaa Xaa Xaa Xaa Xaa Xaa Xaa
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Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
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<221> VARIANT
<222> (25)..(25)
<223> wherein Xaa is a hydrophobic amino acid

<400> 42
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1          5          10          15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
20          25

<210> 43
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<212> PRT
<213> Artificial

<220>
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<220>
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<220>
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<223> wherein Xaa is a charged amino acid

<220>
<221> VARIANT
<222> (4)..(4)
<223> wherein Xaa is any amino acid

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<221> VARIANT
 <222> (5)..(5)
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 <223> wherein Xaa is a hydrophobic amino acid

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 <223> wherein Xaa is any amino acid

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 <222> (22)..(23)
 <223> wherein Xaa is a hydrophobic amino acid

 <400> 43

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
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<210> 44
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 <213> Artificial

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<220>
 <221> VARIANT
 <222> (23)..(23)
 <223> wherein Xaa is a hydrophobic amino acid

<400> 44

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 20

<210> 45
<211> 23
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<220>
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<221> misc_feature
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<220>
<221> VARIANT
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<220>
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<400> 45

Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
1				5					10						15	

Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
						20

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<400> 46

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
20

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<221> VARIANT

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<400> 47

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
20 25

<210> 48

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<221> misc_feature

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<220>
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<222> (3)..(3)
<223> wherein Xaa is any amino acid

<220>
<221> VARIANT
<222> (4)..(4)
<223> wherein Xaa is a hydrophobic amino acid

<220>
<221> VARIANT
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<221> VARIANT
<222> (7)..(8)
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<221> VARIANT
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<221> VARIANT
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<223> wherein Xaa is any amino acid

<220>
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<400> 48

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 20

<210> 49
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 <221> VARIANT
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<220>
 <221> VARIANT
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<220>
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 <223> wherein Xaa is a hydrophobic amino acid

<400> 49

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 20

<210> 50
 <211> 26
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 <213> Artificial

<220>
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<220>
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<220>
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 <223> wherein Xaa is any amino acid

<220>
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<220>
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<222> (5)..(5)
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<220>
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<223> wherein Xaa is a hydrophobic amino acid

<220>
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<222> (7)..(7)
<223> wherein Xaa is a hydrophobic amino acid, or no amino acid is present

<220>
<221> VARIANT
<222> (8)..(8)
<223> wherein Xaa is any amino acid, or no amino acid is present

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<222> (14)..(14)
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<223> wherein Xaa is a hydrophobic amino acid

<220>
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<222> (19)..(19)
<223> wherein Xaa is a hydrophobic amino acid, or is not present

<220>
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<220>
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<220>
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<400> 50

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1				5					10						15	

Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
			20					25	

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 <222> (7)..(7)
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<223> wherein xaa is a hydrophobic amino acid, or not present
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 <223> wherein Xaa is any amino acid, or is not present
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 <221> VARIANT
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 <221> VARIANT
 <222> (21)..(21)
 <223> wherein Xaa is a hydrophobic amino acid, or is not present
 <220>
 <221> VARIANT
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 <221> VARIANT
 <222> (23)..(24)
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 <220>
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 <222> (27)..(28)
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 <400> 51

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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 20 25

<210> 52
 <211> 23
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<220>
 <221> VARIANT
 <222> (22)..(23)
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<400> 52

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 20

<210> 53
 <211> 205
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<220>
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<400> 53

Met Lys Asn Tyr His Asp Ile Val Leu Ala Leu Ala Gly Val Cys Gln
 1 5 10 15

Ser Ala Lys Leu Val His Gln Leu Ala Thr Glu Ser Arg Ala Asp Ser
 20 25 30

Glu Thr Phe Leu Thr Ala Leu Asn Ser Leu Phe Ile Thr Gln Pro Gln
 35 40 45

Arg Ile Glu Asp Val Phe Gly Gly Glu Val Arg His Leu Lys Leu Gly
 50 55 60

Leu Glu Thr Leu Ile His Gln Leu Asn Ala Gln Gly Asp Gln Asn Leu
 65 70 75 80

Thr Arg Tyr Trp Leu Ser Leu Leu Ala Leu Glu Gly Lys Leu Ser Lys
 85 90 95

Asn Ser Asp Ala Lys Gln Thr Leu Gly Asn Arg Ile Ser Arg Leu Lys
 100 105 110

Glu Gln Glu Ile His Tyr Ala Arg Asp Ser Glu Thr Met Leu Ser Ile
 115 120 125

Met Ala Asn Ile Tyr Ser Asp Ile Ile Ser Pro Leu Gly Lys Lys Ile
 130 135 140

His Ile Leu Gly Ser Pro Asp Tyr Leu Arg Gln Glu Leu Val Gln Asn
 145 150 155 160

Lys Ile Arg Ala Val Leu Leu Ala Gly Ile Arg Ser Ala Val Leu Trp
 165 170 175

Lys Gln Met Gly Gly Thr Lys Trp Gln Ile Leu Phe Phe Arg Arg Lys
 180 185 190

Leu Leu Ala Thr Ala Lys Gln Ile Tyr Ser Ser Ile Tyr
 195 200 205

<210> 54
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<220>
 <223> Penetrating peptide consensus sequence

<400> 54

Met Ala Asn Tyr Tyr Asp Ile Thr Leu Ala Leu Ala Gly Val Cys Gln
 1 5 10 15

Ala Ala Lys Leu Val Gln Gln Phe Ala His Glu Gly Gln Ala Asp Gln
 20 25 30

Ala Ala Phe Glu Thr Ser Leu Asn Thr Leu Leu Gln Ile Tyr Pro Glu
 35 40 45

Asp Thr Leu Ala Val Phe Gly Gly Lys Ala Gln Asn Leu Lys Leu Gly
 50 55 60

Leu Glu Thr Leu Leu Glu Gln Met His Gly Thr Gly Ser Asp Leu Ser
 65 70 75 80

Arg Tyr Trp Ile Ser Leu Leu Ala Leu Glu Ser Lys Leu Asn Lys Asp
 85 90 95

Pro His Ala Lys Ala Glu Leu Ala Arg Arg Ile Gln Tyr Leu Pro Thr
 100 105 110

Gln Leu Glu His Tyr Asp Leu Leu Asp Glu Gln Met Leu Ser Thr Leu
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120

125

Ala Ser Ile Tyr Val Asp Val Ile Ser Pro Leu Gly Lys Lys Ile Gln
 130 135 140

Val Thr Gly Ser Thr Leu Tyr Leu Gln Gln Leu Ala Met His His Arg
 145 150 155 160

Ile Arg Ala Cys Leu Leu Ala Gly Ile Arg Ser Ala Val Leu Trp Arg
 165 170 175

Gln Val Gly Gly Thr Lys Trp Gln Val Leu Phe Ser Arg Arg Lys Ile
 180 185 190

Ile Ala Met Ala Lys Gln Ile Tyr Ser Ser Leu
 195 200

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 <212> PRT
 <213> Artificial

<220>
 <223> Penetrating peptide consensus sequence

<400> 55

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 1 5 10 15

Gln Ser Ala Arg Leu Val Gln Gln Leu Ala His Gln Gly His Cys Asp
 20 25 30

Ala Asp Ala Leu His Val Ser Leu Asn Ser Ile Ile Asp Met Asn Pro
 35 40 45

Ser Ser Thr Leu Ala Val Phe Gly Gly Ser Glu Ala Asn Leu Arg Val
 50 55 60

Gly Leu Glu Thr Leu Leu Gly Val Leu Asn Ala Ser Ser Arg Gln Gly
 65 70 75 80

Leu Asn Ala Glu Leu Thr Arg Tyr Thr Leu Ser Leu Met Val Leu Glu
 85 90 95

Arg Lys Leu Ser Ser Ala Lys Gly Ala Leu Asp Thr Leu Gly Asn Arg
 100 105 110

Ile Asn Gly Leu Gln Arg Gln Leu Glu His Phe Asp Leu Gln Ser Glu
 115 120 125

Thr Leu Met Ser Ala Met Ala Ala Ile Tyr Val Asp Val Ile Ser Pro
 130 135 140

Leu Gly Pro Arg Ile Gln Val Thr Gly Ser Pro Ala Val Leu Gln Ser
 145 150 155 160

Pro Gln Val Gln Ala Lys Val Arg Ala Thr Leu Leu Ala Gly Ile Arg
 165 170 175

Ala Ala Val Leu Trp His Gln Val Gly Gly Gly Arg Leu Gln Leu Met
 180 185 190

Phe Ser Arg Asn Arg Leu Thr Thr Gln Ala Lys Gln Ile Leu Ala His
 195 200 205

Leu Thr Pro Glu Leu
 210

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 <223> Penetrating peptide consensus sequence

<400> 56

Met Ala Asn Ala Ile Tyr Asp Arg Thr Ile Ala Phe Ala Gly Ile Cys
 1 5 10 15

Gln Ala Val Ala Leu Val Gln Gln Val Ala Lys Asn Gly Tyr Cys Asp
 20 25 30

Ser Asp Ala Phe Glu Thr Ser Leu Lys Ala Ile Thr Cys Thr Asn Pro
 35 40 45

Ser Asn Thr Leu Glu Val Phe Gly His Glu Ser Gln Leu Lys Leu Gly
 50 55 60

Leu Glu Cys Leu Val Lys Gly Ile Asp Ser Thr Pro Ser Gly Ser Glu
 65 70 75 80

Ile Thr Arg Tyr Leu Ile Ser Leu Met Ala Leu Glu Arg Lys Leu Ser
 85 90 95

Gly Arg Arg Asp Ala Met Ser Gln Leu Gly Asp Arg Ile Gln Met Ile
 100 105 110

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Glu Arg Gln Leu Asp His Phe Asp Leu Phe Asp Asp Gln Met Ile Ser
115 120 125

Asn Leu Ala Ser Ile Tyr Leu Asp Val Ile Ser Pro Ile Gly Pro Arg
130 135 140

Ile Gln Val Thr Gly Thr Pro Ala Val Leu Gln Gln Thr Ala Asn Gln
145 150 155 160

His Lys Val Arg Ala Leu Leu Leu Ser Gly Ile Arg Cys Ala Val Leu
165 170 175

Trp Arg Gln Val Gly Gly Arg Arg Arg His Leu Ile Phe Gly Arg Lys
180 185 190

Lys Met Ile Glu Gln Ala Gln Ile Leu Leu Ala Arg
195 200

<210> 57
<211> 211
<212> PRT
<213> Artificial

<220>
<223> Penetrating peptide consensus sequence

<400> 57

Met Lys Lys Ile His Leu Ile Thr Leu Ser Leu Ala Gly Ile Cys Gln
1 5 10 15

Ser Ala His Leu Val Gln Gln Leu Ala Tyr Ser Gly Lys Cys Asp Ser
20 25 30

Asn Ala Phe Ser Ile Cys Leu Lys Ser Ile Leu Glu Ile Asn Pro Thr
35 40 45

Ser Phe Ile Ala Ile Tyr Gly Asn His Glu Lys Asn Leu Ile Ile Gly
50 55 60

Leu Glu Ile Leu Leu Ser Thr Leu Thr Phe Ser Ser Phe Ser Tyr Ser
65 70 75 80

Tyr Ile Glu Leu Ile Lys Tyr Ile Ser Asn Met Met Ile Ile Glu Lys
85 90 95

Lys Leu Lys Lys Ser Arg Thr Ala Ile Tyr Ser Leu Lys Asn Lys Ile
100 105 110

Ser Val Ile Ser Ser Glu Tyr Tyr Leu Asn Tyr Asn Ile Lys Asn Leu
 115 120 125

Thr Arg Lys Leu Gly Glu Leu Tyr Leu Glu Ile Ile Ser Ser Leu Gly
 130 135 140

Ser Arg Ile Val Ile Lys Gly Ile Lys Asp Phe Leu Gln Asp His Gln
 145 150 155 160

Ile Gln Glu Lys Ile Arg Cys Leu Leu Phe Ser Gly Ile Arg Ala Ile
 165 170 175

Val Leu Trp Lys Gln Tyr Gly Gly Asn Gln Leu Gln Leu Ile Tyr Phe
 180 185 190

Arg Tyr Phe Ile Ile Lys Lys Ala Lys Lys Ile Leu Tyr His Leu Lys
 195 200 205

Asp Ala Thr
 210

<210> 58
 <211> 206
 <212> PRT
 <213> Artificial

<220>
 <223> Penetrating peptide consensus sequence

<400> 58

Met Ser Asp Pro Arg Gln Gln Leu Ile Ala Leu Gly Ala Val Phe Glu
 1 5 10 15

Ser Ala Ala Leu Val Asp Lys Leu Ala Arg Thr Gly Gln Ile Ser Glu
 20 25 30

Ala Pro Leu Gly Cys Met Leu Gly Ser Leu Leu Ala Arg Asn Pro Ala
 35 40 45

Ser Thr Leu Asp Val Tyr Gly Gly Asp Ser Leu Asn Leu Arg Asp Gly
 50 55 60

Phe Lys Ala Leu Ala Ser Ala Leu Glu Arg Lys Pro Gly Ser Leu Gln
 65 70 75 80

Arg Glu Pro Leu Arg Tyr Ala Leu Ala Met Leu Thr Leu Glu Arg Gln
 85 90 95

Leu Asp Lys Arg Gly Asp Met Leu Asp Leu Ile Gly Gln Arg Leu Asp
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100

105

110

Gln Val Glu Gln Gln Val Gln His Phe Gly Leu Val His Glu Asn Val
 115 120 125

Ile Ala Ser Phe Ala Ser Ile Tyr Gln Asp Thr Leu Ser Thr Phe Arg
 130 135 140

Gln Arg Ile Gln Val His Gly Asp Met Arg His Leu Gln Val Ser Ser
 145 150 155 160

Asn Ala Ala Arg Ile Arg Ala Leu Leu Leu Ala Gly Ile Arg Ser Ala
 165 170 175

Arg Leu Trp Arg Gln Leu Gly Gly Ser Arg Trp Gln Met Val Phe Ser
 180 185 190

Arg Arg Arg Leu Leu Asn Glu Leu Tyr Pro Leu Leu Arg Gly
 195 200 205

<210> 59

<211> 204

<212> PRT

<213> Artificial

<220>

<223> Penetrating peptide consensus sequence

<400> 59

Met Asn Ala Leu Ile Asp Asn Arg Val Leu Ala Leu Ala Gly Val Val
 1 5 10 15

Gln Ala Leu Gln Gln Val Arg Gln Ile Ala Glu Thr Gly Gln Ser Glu
 20 25 30

Thr Ser Ala Val Arg Thr Ala Ile Asp Ser Val Leu Arg Ile Asp Ala
 35 40 45

Glu Ser Pro Glu Ala Val Tyr Gly Gly Ile Arg Asp Leu Thr Gln Gly
 50 55 60

Leu Gln Leu Leu His Asp Tyr Phe Gly Asn Gln Leu His Asp Gln Leu
 65 70 75 80

Leu Pro Arg Leu Thr Leu Ala Val Leu Gln Leu Glu Arg Arg Phe Ile
 85 90 95

Arg Asp Thr Ser Ile Val Ala Ala Val Ser Ala Gly Ile Thr Gln Ala
 100 105 110

Ala His Gln Val Glu Gln Thr Gly Asp Ser Ala His Pro Glu Val Leu
 115 120 125

Ser Thr Leu Gly Ala Leu Tyr Ala Asn Thr Ile Ser His Leu Arg Pro
 130 135 140

Arg Ile Ile Val Gln Gly Asn Pro His Tyr Leu Gly Gln Ala Gly Val
 145 150 155 160

Val Ala Glu Ile Arg Ala Met Leu Leu Ala Ala Leu Arg Ser Ala Val
 165 170 175

Leu Trp Arg Gln Leu Asn Gly Asn Leu Leu Asp Phe Leu Leu Ala Lys
 180 185 190

Arg Ala Met Ala Ala Ala Thr Glu Arg Ala Leu Arg
 195 200

<210> 60
 <211> 5
 <212> PRT
 <213> Artificial

<220>
 <223> Fully conserved "strong" amino acid residue chain
 <400> 60

Asn Arg Glu Gln Lys
 1 5

<210> 61
 <211> 4
 <212> PRT
 <213> Artificial

<220>
 <223> Fully conserved "strong" amino acid residue chain
 <400> 61

Asn His Gln Lys
 1

<210> 62
 <211> 4
 <212> PRT
 <213> Artificial

<220>
 <223> Fully conserved "strong" amino acid residue chain
 <400> 62

Asn Asp Glu Gln
1

<210> 63
<211> 4
<212> PRT
<213> Artificial

<220>
<223> Fully conserved "strong" amino acid residue chain

<400> 63

Gln His Arg Lys
1

<210> 64
<211> 4
<212> PRT
<213> Artificial

<220>
<223> Fully conserved "strong" amino acid residue chain

<400> 64

Met Ile Leu Val
1

<210> 65
<211> 4
<212> PRT
<213> Artificial

<220>
<223> Fully conserved "strong" amino acid residue chain

<400> 65

Met Ile Leu Phe
1

<210> 66
<211> 4
<212> PRT
<213> Artificial

<220>
<223> Fully conserved "weak" amino acid residue chain

<400> 66

Ser Thr Asn Lys
1

<210> 67
<211> 4

<212> PRT
 <213> Artificial

<220>
 <223> Fully conserved "weak" amino acid residue chain

<400> 67

Ser Thr Pro Ala
 1

<210> 68
 <211> 4
 <212> PRT
 <213> Artificial

<220>
 <223> Fully conserved "weak" amino acid residue chain

<400> 68

Ser Gly Asn Asp
 1

<210> 69
 <211> 6
 <212> PRT
 <213> Artificial

<220>
 <223> Fully conserved "weak" amino acid residue chain

<400> 69

Ser Asn Asp Glu Gln Lys
 1 5

<210> 70
 <211> 6
 <212> PRT
 <213> Artificial

<220>
 <223> Fully conserved "weak" amino acid residue chain

<400> 70

Asn Asp Glu Gln His Lys
 1 5

<210> 71
 <211> 6
 <212> PRT
 <213> Artificial

<220>
 <223> Fully conserved "weak" amino acid residue chain

<400> 71

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Asn Glu Gln His Arg Lys
1 5

<210> 72
<211> 23
<212> PRT
<213> Bacillus subtilis

<400> 72

Asn Leu Thr Lys Thr Ser Leu Leu Leu Ala Gly Leu Cys Thr Ala Ala
1 5 10 15

Gln Met Val Phe Val Thr His
20